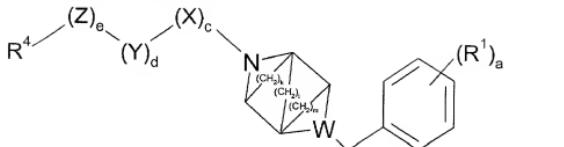


CLAIMS

1. A compound of the formula



5 or the pharmaceutically acceptable salt and pro-drugs thereof; wherein

a is 1, 2, 3, 4 or 5;

c is 0 or 1;

d is 1, 2, 3, 4 or 5;

k is 0, 1, 2, 3 or 4; l is 0, 1, 2, 3 or 4; m is 0, 1, 2, 3, or 4; k, l and m cannot all be 0

10 and if m and/or k are not 0, then l must be 0;

W is CH or N;

X is C(O), C(S) or CH_2 ;

Y is CH_2 ;

Z is oxygen, NR^9 or $CR^{11}R^{12}$;

15 each R^1 is independently selected from hydrogen, hydroxy, hydroxysulfonyl, halo, (C_1-C_6) alkyl, mercapto, mercapto(C_1-C_6)alkyl, (C_1-C_6) alkylthio, (C_1-C_6) alkylsulfinyl, (C_1-C_6) alkylsulfonyl, (C_1-C_6) alkylthio(C_1-C_6)alkyl, (C_1-C_6) alkylsulfinyl(C_1-C_6)alkyl, (C_1-C_6) alkylsulfonyl(C_1-C_6)alkyl, (C_1-C_6) alkoxy, (C_6-C_{10}) aryloxy, halo(C_1-C_6)alkyl, trifluoromethyl, formyl, formyl(C_1-C_6)alkyl, nitro, nitroso, cyano, (C_6-C_{10}) aryl(C_1-C_6)alkoxy, halo(C_1-C_6)alkoxy, trifluoromethoxy, (C_3-C_7) cycloalkyl, (C_3-C_7) cycloalkyl(C_1-C_6)alkyl, hydroxy(C_3-C_7)cycloalkyl(C_1-C_6)alkyl, (C_3-C_7) cycloalkylamino, (C_3-C_7) cycloalkylamino(C_1-C_6)alkyl, $((C_3-C_7)$ cycloalkyl)(C_1-C_6)alkyl)amino, $((C_3-C_7)$ cycloalkyl(C_1-C_6)alkyl)amino(C_1-C_6)alkyl, cyano(C_1-C_6)alkyl, (C_2-C_7) alkenyl, (C_2-C_7) alkynyl, (C_6-C_{10}) aryl, (C_6-C_{10}) aryl(C_1-C_6)alkyl, (C_6-C_{10}) aryl(C_2-C_6)alkenyl, hydroxy(C_1-C_6)alkyl, hydroxy(C_6-C_{10})aryl(C_1-C_6)alkyl, hydroxy(C_1-C_6)alkylthio(C_1-C_6)alkyl,

20 hydroxy(C_2-C_6)alkenyl, hydroxy(C_2-C_6)alkynyl, (C_1-C_6) alkoxy(C_1-C_6)alkyl, (C_1-C_6) alkoxy(C_6-C_{10})aryl(C_1-C_6)alkyl, (C_6-C_{10}) aryloxy(C_1-C_6)alkyl, (C_6-C_{10}) aryl(C_1-C_6)alkyl, amino, (C_1-C_6) alkylamino, $((C_1-C_6)$ alkyl)amino, (C_6-C_{10}) aryl(C_1-C_6)alkylamino, (C_6-C_{10}) aryl(C_1-C_6)alkyl, hydroxy(C_1-C_6)alkylamino(C_1-C_6)alkyl, (C_6-C_{10}) aryl(C_1-C_6)alkylamino, (C_6-C_{10}) aryl(C_1-C_6)alkyl, (C_1-C_6) alkylamino(C_1-C_6)alkyl,

25 $((C_1-C_6)$ alkyl)amino(C_1-C_6)alkyl, (C_1-C_6) alkylcarbonylamino, $((C_1-C_6)$ alkylcarbonyl)((C_1-C_6)alkyl)amino, (C_1-C_6) alkylcarbonylaminoo(C_1-C_6)alkyl, $((C_1-C_6)$ alkylcarbonyl)((C_1-C_6)alkyl)amino, (C_1-C_6) alkylcarbonylaminoo(C_1-C_6)alkyl, $((C_1-C_6)$ alkylcarbonyl)((C_1-C_6)alkyl)amino, (C_1-C_6) alkoxycarbonylamino, (C_1-C_6) alkoxycarbonylaminoo(C_1-C_6)alkyl,

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C_6)heteroaryloxy, (C_2-C_6) heterocycloalkyl, carboxy(C_1-C_6)alkoxy, (C_1-C_6)alkylsulfonylaminocarbonyl(C_1-C_6)alkoxy, (C_1-C_6)alkylsulfonylaminocarbonyl(C_1-C_6)alkoxy, (C_2-C_6)heteroaryl(C_1-C_6)alkoxy, carboxy(C_1-C_6)alkylaminocarbonyl(C_2-C_6)alkoxy, amino(C_2-C_6)alkoxy, (aminocarbonyl)(hydroxy)amino, (C_1-C_6)alkylaminocarbonyl(C_2-C_6)alkoxy, $((C_1-C_6)$ alkyl) $_2$ amino(C_2-C_6)alkoxy, (C_1-C_6)alkyl, (C_1-C_6)alkylcarbonylaminocarbonyl(C_2-C_6)alkoxy, aminocarbonylaminocarbonyl(C_2-C_6)alkoxy, (C_1-C_6)alkylaminocarbonylaminocarbonyl(C_2-C_6)alkoxy, amino(C_2-C_6)alkoxycarbonylaminocarbonyl, (C_1-C_6)alkylaminocarbonyl(C_2-C_6)alkoxy, carboxy(C_1-C_6)alkylaminocarbonyl, (C_2-C_6)heteroarylaminocarbonyl(C_2-C_6)alkoxy, barbituryl, (C_1-C_6)alkylcarbonylaminocarbonyl(C_1-C_6)alkylaminocarbonyl, amino(C_1-C_6)alkylcarbonylaminocarbonyl where

5 the (C_1-C_6)alkyl is optionally substituted with one or two groups selected from hydrogen, amino, hydroxyl, (C_1-C_6)alkoxy, carboxy, further substituted (C_2-C_6)heteroaryl, (C_6-C_{10})aryl, (C_2-C_6)heterocycloalkyl, and cycloalkyl, or the two groups together make up a carbocycle; and R¹⁹carbonylaminocarbonyl where R¹⁹ is a nitrogen containing (C_2-C_6)heterocycloalkyl which is 10 optionally substituted further with one or two groups selected from (C_1-C_6)alkyl, (C_2-C_6)alkoxy and hydroxy;

15 R⁹ is selected from the group consisting of hydrogen, (C_1-C_6)alkyl, (C_6-C_{10})aryl, (C_6-C_{10})aryl(C_1-C_6)alkyl, (C_1-C_6)alkylcarbonyl, (C_1-C_6)alkylcarbonyl(C_1-C_6)alkyl, (C_6-C_{10})aryl(C_1-C_6)alkylcarbonyl, (C_6-C_{10})aryl(C_1-C_6)alkylcarbonyl(C_1-C_6)alkyl, aminocarbonyl, (C_1-C_6)alkylaminocarbonyl, ((C_1-C_6) alkyl) $_2$ aminocarbonyl and (C_1-C_6)alkoxycarbonyl; and

20 R¹¹ and R¹² are each independently selected from the group consisting of hydrogen, (C_1-C_6)alkyl, (C_6-C_{10})aryl, (C_6-C_{10})aryl(C_1-C_6)alkyl, hydroxy, (C_1-C_6)alkoxy, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy(C_1-C_6)alkyl, amino, (C_1-C_6)alkylamino, $((C_1-C_6)$ alkyl) $_2$ amino, (C_1-C_6)alkylcarbonylaminocarbonyl, (C_3-C_8)cycloalkylcarbonylaminocarbonyl, (C_3-C_8)cycloalkyl(C_1-C_6)alkylcarbonylaminocarbonyl, (C_1-C_6)alkoxycarbonylaminocarbonyl, (C_1-C_6)alkylsulfonylaminocarbonyl, (C_6-C_{10})aryl(C_1-C_6)alkylcarbonylaminocarbonyl, (C_1-C_6)alkoxycarbonyl(C_1-C_6)alkylcarbonylaminocarbonyl, ((C_6-C_{10}) aryl(C_1-C_6)alkylcarbonyl)((C_1-C_6) alkyl)amino, (C_1-C_6)alkylcarbonylaminocarbonyl(C_1-C_6)alkyl, (C_3-C_8)cycloalkylcarbonylaminocarbonyl(C_1-C_6)alkyl, (C_1-C_6)alkoxycarbonylaminocarbonyl(C_1-C_6)alkyl, (C_2-C_6)heterocycloalkylcarbonylaminocarbonyl(C_1-C_6)alkyl, (C_6-C_{10})aryl(C_1-C_6)alkylcarbonylaminocarbonyl(C_1-C_6)alkyl, (C_2-C_6)heteroarylcarbonylaminocarbonyl(C_1-C_6)alkyl, (C_6-C_{10})aryl(C_1-C_6)alkylsulfonylaminocarbonyl, (C_1-C_6)alkylsulfonylaminocarbonyl(C_1-C_6)alkyl, aminocarbonylaminocarbonyl, (C_1-C_6)alkylaminocarbonylaminocarbonyl, halo(C_1-C_6)alkylaminocarbonylaminocarbonyl, ((C_1-C_6) alkyl) $_2$ aminocarbonylaminocarbonyl(C_1-C_6)alkyl, halo(C_1-C_6)alkylaminocarbonylaminocarbonyl(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, (C_1-C_6)alkylaminocarbonyl(C_1-C_6)alkyl, ((C_1-C_6) alkyl) $_2$ amino(C_1-C_6)alkyl, carboxy(C_1-C_6)alkyl, (C_1-C_6)alkoxycarbonyl(C_1-C_6)alkyl, aminocarbonyl(C_1-C_6)alkyl and (C_1-C_6)alkylaminocarbonyl(C_1-C_6)alkyl.

C_6)alkylureido, (C_1-C_6) alkylcarbonyl, (C_1-C_6) alkylsulfonylamino, (C_1-C_6) alkylsulfonylamino(C_1-C_6)alkylaminocarbonyl, aminosulfonyl, aminocarbonyl, ureido(C_1-C_6)alkylaminocarbonyl, aminocarbonyl(C_1-C_6)alkylaminocarbonyl, aminocarbonyl(C_1-C_6)alkylcarbonylamino, ureido(C_1-C_6)alkylcarbonylamino, (C_1-C_6) alkylcarbonylamino(C_1-C_6)alkylcarbonylamino, (C_1-C_6) alkylcarbonylamino(C_1-C_6)alkylaminocarbonylamino, ureido(C_1-C_6)alkylcarbonylamino, ureido, halo(C_1-C_6)alkylsulfonylamino, (C_1-C_6) alkylcarbonylamino(C_1-C_6)alkylaminocarbonyl.

C_6)alkylcarbonylamino(C_1 - C_6)alkylcarbonylamino, $(C_1$ - C_6)alkylcarbonylamino(C_1 - C_6)alkylaminocarbonylamino, ureido(C_1 - C_6)alkylcarbonylamino, ureido, halo(C_1 - C_6)alkylsulfonylamino, (C_1 - C_6)alkylcarbonylamino(C_1 - C_6)alkylaminocarbonyl.

8. Salts of a compound according to claim 1, where pharmaceutically acceptable counter-ions for acidic compounds are selected from alkali metal cations, alkaline earth metal cations ammonium or water-soluble amine addition salts, N-methylglucamine-(meglumine), the lower alkanolammonium and other base salts of pharmaceutically acceptable organic amines; and pharmaceutically acceptable salts selected from hydrochloride, hydrobromide, hydroiodide, nitrate, sulfate, bisulfate, phosphate, acid phosphate, acetate, lactate, citrate, acid citrate, tartrate, bitartrate, succinate, maleate, fumarate, gluconate, saccharate, benzoate, methanesulfonate, ethanesulfonate, benzenesulfonate, p-toluenesulfonate and pamoatesalts.

9. A pharmaceutical composition for treating or preventing a disorder or condition selected from autoimmune diseases, rheumatoid arthritis, type I diabetes (recent onset), lupus, inflammatory bowel disease, optic neuritis, psoriasis, multiple sclerosis, polymyalgia rheumatica, uveitis, and vasculitis, acute and chronic inflammatory conditions osteoarthritis, adult Respiratory Distress Syndrome, Respiratory Distress Syndrome of infancy, ischemia reperfusion injury, glomerulonephritis, and chronic obstructive pulmonary disease (COPD) allergic conditions, asthma and atopic dermatitis, inflammation associated with infection, viral inflammation, influenza, hepatitis and Guillain-Barre, chronic bronchitis, chronic or acute tissue, cell, and solid organ transplant rejection, xeno-transplantation, atherosclerosis, restenosis, HIV infectivity (co-receptor usage), and granulomatous diseases, sarcoidosis, leprosy and tuberculosis, and sequelae associated with cancers, multiple myeloma; limiting the production of cytokines and/or TNF at inflammatory sites, as a consequence of decreasing cell infiltration; for treating diseases and/or congestive heart failure, linked to TNF and IL-1 and for treating pulmonary emphysema or dyspnea associated therewith, emphysema; HIV-1, HIV-2, HIV-3; cytomegalovirus (CMV), adenoviruses, Herpes viruses (*Herpes zoster* and *Herpes simplex*), for treating sequelae associated with infection where such infection induces production of detrimental inflammatory cytokines and/or TNF, fungal meningitis, joint tissue damage, hyperplasia, pannus formation and bone resorption, psoriatic arthritis, hepatic failure, bacterial meningitis, Kawasaki syndrome, myocardial infarction, acute liver failure, lyme disease, septic shock, cancer, trauma, and malaria, in a mammal, comprising an amount of a compound according to claim 1, or a pharmaceutically acceptable salt or pro-drug thereof, that is effective in treating or preventing such disorder or condition and a pharmaceutically acceptable carrier.

10. A pharmaceutical composition for treating or preventing a disorder or condition that can be treated or prevented by inhibiting chemokine binding to the receptor CCR1 in a

mammal, comprising an amount of a compound according to claim 1, or a pharmaceutically acceptable salt or pro-drug thereof, effective in treating or preventing such disorder or condition and a pharmaceutically acceptable carrier.

11. A method for treating or preventing a disorder or condition selected from
5 autoimmune diseases, rheumatoid arthritis, type I diabetes (recent onset), lupus, inflammatory bowel disease, optic neuritis, psoriasis, multiple sclerosis, polymyalgia rheumatica, uveitis, and vasculitis, acute and chronic inflammatory conditions osteoarthritis, adult Respiratory Distress Syndrome, Respiratory Distress Syndrome of infancy, ischemia reperfusion injury, glomerulonephritis, and chronic obstructive pulmonary disease (COPD)
10 allergic conditions, asthma and atopic dermatitis, inflammation associated with infection, viral inflammation, influenza, hepatitis and Guillain-Barre, chronic bronchitis, chronic or acute tissue, cell, and solid organ transplant rejection, xeno-transplantation, atherosclerosis, restenosis, HIV infectivity (co-receptor usage), and granulomatous diseases, sarcoidosis, leprosy and tuberculosis, and sequelae associated with cancers, multiple myeloma; limiting
15 the production of cytokines and/or TNF at inflammatory sites, as a consequence of decreasing cell infiltration; for treating diseases and/or congestive heart failure, linked to TNF and IL-1 and for treating pulmonary emphysema or dyspnea associated therewith, emphysema; HIV-1, HIV-2, HIV-3; cytomegalovirus (CMV), adenoviruses, Herpes viruses (*Herpes zoster* and *Herpes simplex*), for treating sequelae associated with infection where
20 such infection induces production of detrimental inflammatory cytokines and/or TNF, fungal meningitis, joint tissue damage, hyperplasia, pannus formation and bone resorption, psoriatic arthritis, hepatic failure, bacterial meningitis, Kawasaki syndrome, myocardial infarction, acute liver failure, lyme disease, septic shock, cancer, trauma, and malaria, in a mammal, comprising administering to a mammal in need of such treatment or prevention an amount of a compound
25 according to claim 1, or a pharmaceutically acceptable salt or pro-drug thereof, that is effective in treating or preventing such disorder or condition.

12. A method for treating or preventing a disorder or condition that can be treated or prevented by antagonizing the CCR1 receptor in a mammal, comprising administering to a mammal in need of such treatment or prevention an amount of a compound according to claim
30 1, or a pharmaceutically acceptable salt or pro-drug thereof, that is effective in treating or preventing such disorder or condition.

13. A pharmaceutical composition for treating or preventing a disorder or condition selected from autoimmune diseases, rheumatoid arthritis, type I diabetes (recent onset), lupus, inflammatory bowel disease, optic neuritis, psoriasis, multiple sclerosis, polymyalgia rheumatica, uveitis, and vasculitis, acute and chronic inflammatory conditions osteoarthritis, adult Respiratory Distress Syndrome, Respiratory Distress Syndrome of infancy, ischemia reperfusion injury, glomerulonephritis, and chronic obstructive pulmonary disease (COPD)
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allergic conditions, asthma and atopic dermatitis, inflammation associated with infection, viral inflammation, influenza, hepatitis and Guillain-Barre, chronic bronchitis, chronic or acute tissue, cell, and solid organ transplant rejection, xeno-transplantation, atherosclerosis, restenosis, HIV infectivity (co-receptor usage), and granulomatous diseases, sarcoidosis, 5 leprosy and tuberculosis, and sequelae associated with cancers, multiple myeloma; limiting the production of cytokines and/or TNF at inflammatory sites, as a consequence of decreasing cell infiltration; for treating diseases and/or congestive heart failure, linked to TNF and IL-1 and for treating pulmonary emphysema or dyspnea associated therewith, emphysema; HIV-1, HIV-2, HIV-3; cytomegalovirus (CMV), adenoviruses, Herpes viruses 10 (*Herpes zoster* and *Herpes simplex*), for treating sequelae associated with infection where such infection induces production of detrimental inflammatory cytokines and/or TNF, fungal meningitis, joint tissue damage, hyperplasia, pannus formation and bone resorption, psoriatic arthritis, hepatic failure, bacterial meningitis, Kawasaki syndrome, myocardial infarction, acute liver failure, lyme disease, septic shock, cancer, trauma, and malaria, in a mammal, 15 comprising a CCR1 receptor antagonizing effective amount of a compound according to claim 1, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

14. A pharmaceutical composition for treating or preventing a disorder or condition that can be treated or prevented by antagonizing the CCR1 receptor in a mammal, comprising a CCR1 receptor antagonizing effective amount of a compound according to claim 1, or a pharmaceutically acceptable salt or pro-drug thereof, and a pharmaceutically acceptable carrier.

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